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MeSH Descriptor Data

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MeSH Heading	Guanabenz
Tree Number	D02.078.370.435
Scope Note	An alpha-2 selective adrenergic agonist used as an antihypertensive agent.
Entry Term	2,6-Dichlorobenzylideneaminoguanidine
Entry Term	BR-750
Entry Term	Guanabenz Acetate
Entry Term	Guanabenz Monoacetate
Entry Term	WY-8678
Entry Term	Wytensin
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Adrenergic alpha-Agonists
Pharm. Action	Antihypertensive Agents
Pharm. Action	Sympatholytics
CAS Type 1 Name	Hydrazinecarboximidamide, 2-((2,6-dichlorophenyl)methylene)-
Registry Number	5051-62-7
Related Number	23256-50-0 (monoacetate)
Previous Indexing	Guanidines (1973-1974)
Previous Indexing	Imines (1973-1974)
History Note	91(75); was see under GUANIDINES 1975-90
Unique ID	D006143

MeSH Tree Structures

PDR® entry for
Catapres-TTS (Boehringer Ingelheim)

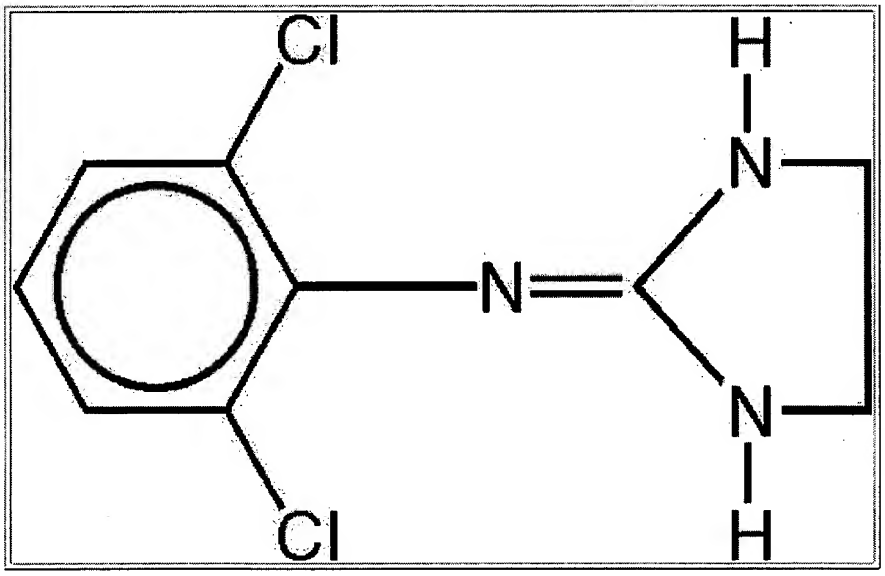
Description

Programmed delivery *in vivo* of 0.1, 0.2, or 0.3 mg clonidine per day, for one week.

Prescribing Information

DESCRIPTION

Catapres-TTS® (clonidine) is a transdermal system providing continuous systemic delivery of clonidine for 7 days at an approximately constant rate. Clonidine is a centrally acting alpha-agonist hypotensive agent. It is an imidazoline derivative with the chemical name 2, 6-dichloro-N-2-imidazolidinylidenebenzenamine and has the following chemical structure:



(clonidine)

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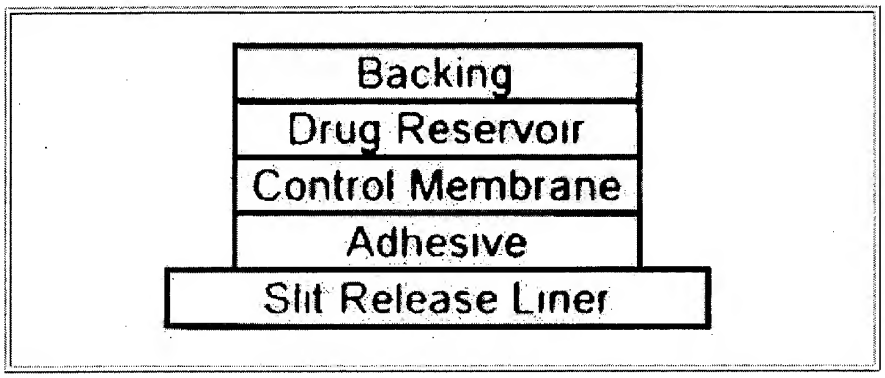
System Structure and Components Catapres-TTS is a multilayered film, 0.2 mm thick, containing clonidine as the active agent. The system areas are 3.5 cm^2 (CATAPRES-TTS-1), 7.0 cm^2 (CATAPRES-TTS-2) and 10.5 cm^2 (CATAPRES-TTS-3) and the amount of drug released is directly proportional to the area (See Release Rate Concept). The composition per unit area is the same for all three doses.

Proceeding from the visible surface towards the surface attached to the skin, there are four consecutive layers: 1) a backing layer of pigmented polyester film; 2) a drug reservoir of clonidine, mineral oil, polyisobutylene, and colloidal silicon dioxide; 3) a microporous polypropylene membrane that controls the rate of delivery of clonidine from the system to the skin surface; 4) an adhesive formulation of clonidine, mineral oil, polyisobutylene, and colloidal silicon dioxide. Prior to use, a protective slit release liner of polyester that covers the adhesive layer is removed.

Cross section of the system:



Release Rate Concept Catapres-TTS is programmed to release clonidine at an approximately constant rate for 7 days. The energy for drug release is derived from the concentration gradient existing between a saturated solution of drug in the system and the much lower concentration prevailing in the skin. Clonidine flows in the direction of the lower concentration at a constant rate, limited by the rate-controlling membrane, so long as a saturated solution is maintained in the drug reservoir.

Following system application to intact skin, clonidine in the adhesive layer saturates the skin site below the system. Clonidine from the drug reservoir then begins to flow through the rate-controlling membrane and the adhesive layer of the system into the systemic circulation via the capillaries beneath the skin. Therapeutic plasma clonidine levels are achieved 2 to 3 days after initial application of Catapres-TTS.

The 3.5, 7.0, and 10.5 cm^2 systems deliver 0.1, 0.2, and 0.3 mg of clonidine per day, respectively. To ensure constant release of drug for 7 days, the total drug content of the system is higher than the total amount of drug delivered. Application of a new system to a fresh skin site at weekly intervals continuously maintains therapeutic plasma concentrations of clonidine. If the Catapres-TTS is removed and not replaced with a new system, therapeutic plasma clonidine levels will persist for about 8 hours and then decline slowly over several days. Over this time period, blood pressure returns gradually to pretreatment levels.

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CLINICAL PHARMACOLOGY

Clonidine stimulates alpha-adrenoreceptors in the brain stem. This action results in reduced sympathetic outflow from the central nervous system and in decreases in peripheral resistance, renal vascular resistance, heart rate, and blood pressure. Renal blood flow and glomerular filtration rate remain essentially unchanged. Normal postural reflexes are intact; therefore, orthostatic symptoms are mild and infrequent.

Acute studies with clonidine hydrochloride in humans have demonstrated a moderate reduction (15%-20%) of cardiac output in the supine position with no change in peripheral resistance; at a 45° tilt there is a smaller reduction in cardiac output and a decrease of peripheral resistance.

During long-term therapy, cardiac output tends to return to control values, while peripheral resistance remains decreased. Slowing of the pulse rate has been observed in most patients given clonidine, but the

drug does not alter normal hemodynamic responses to exercise.

Tolerance to the antihypertensive effect may develop in some patients, necessitating a reevaluation of therapy.

Other studies in patients have provided evidence of a reduction in plasma renin activity and in the excretion of aldosterone and catecholamines. The exact relationship of these pharmacologic actions to the antihypertensive effect of clonidine has not been fully elucidated.

Clonidine acutely stimulates the release of growth hormone in children as well as adults but does not produce a chronic elevation of growth hormone with long-term use.

Pharmacokinetics The plasma half-life of clonidine is 12.7 ± 7 hours. Following oral administration, about 40-60% of the absorbed dose is recovered in the urine as unchanged drug within 24 hours. The remainder of the absorbed dose is metabolized in the liver.

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INDICATIONS AND USAGE

Catapres-TTS® (clonidine) is indicated in the treatment of hypertension. It may be employed alone or concomitantly with other antihypertensive agents.

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CONTRAINDICATIONS

Catapres-TTS® (clonidine) should not be used in patients with known hypersensitivity to clonidine or to any other component of the therapeutic system.

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WARNINGS

Withdrawal Patients should be instructed not to discontinue therapy without consulting their physician. Sudden cessation of clonidine treatment has, in some cases, resulted in symptoms such as nervousness, agitation, headache, and confusion accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma. The likelihood of such reactions to discontinuation of clonidine therapy appears to be greater after administration of higher doses or continuation of concomitant beta-blocker treatment and special caution is therefore advised in these situations. Rare instances of hypertensive encephalopathy, cerebrovascular accidents and death have been reported after clonidine withdrawal. When discontinuing therapy with Catapres, the physician should reduce the dose gradually over 2 to 4 days to avoid withdrawal symptomatology.

An excessive rise in blood pressure following discontinuation of Catapres-TTS® therapy can be reversed by administration of oral clonidine hydrochloride or by intravenous phentolamine. If therapy is to be discontinued in patients receiving a beta-blocker and clonidine concurrently, the beta-blocker should be withdrawn several days before the gradual discontinuation of Catapres-TTS®.

PRECAUTIONS

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General In patients who have developed localized contact sensitization to Catapres-TTS® (clonidine) continuation of Catapres-TTS or substitution of oral clonidine hydrochloride therapy may be associated with development of a generalized skin rash.

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MeSH Heading	Clonidine
Tree Number	D03.383.374.165
Annotation	an antihypertensive & alpha-2 adrenergic agonist
Scope Note	An alpha-2 adrenergic agonist that crosses the blood-brain barrier. Clonidine's central actions reduce sympathetic tone, resulting in a fall in diastolic and systolic blood pressure and a reduction in heart rate. It also acts peripherally, and this peripheral activity may be responsible for the transient increase in blood pressure seen during rapid intravenous administration. (From Martindale, the Extra Pharmacopoeia, 30th ed, p350)
Entry Term	Catapres
Entry Term	Catapresan
Entry Term	Catapressan
Entry Term	Chlophazolin
Entry Term	Clofelin
Entry Term	Clofenil
Entry Term	Clonidine Hydrochloride
Entry Term	Clopheline
Entry Term	Dixarit
Entry Term	Gemiton
Entry Term	Hemiton
Entry Term	Isoglaucon
Entry Term	Klofelin
Entry Term	Klofenil
Entry Term	M-5041T
Entry Term	ST-155
Entry Term	di-HCl of Clonidine
Entry Term	mono-HBr of Clonidine
Entry Term	mono-HCl of Clonidine
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Adrenergic alpha-Agonists
Pharm. Action	Analgesics
Pharm. Action	Antihypertensive Agents
Pharm. Action	Sympatholytics
CAS Type 1 Name	1H-Imidazol-2-amine, N-(2,6-dichlorophenyl)-4,5-dihydro-
Registry Number	4205-90-7
Related Number	135589-09-2 (mono-HBr)

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MeSH Heading	Guanethidine
Tree Number	D02.078.370.460
Scope Note	An antihypertensive agent that acts by inhibiting selectively transmission in post-ganglionic adrenergic nerves. It is believed to act mainly by preventing the release of norepinephrine at nerve endings and causes depletion of norepinephrine in peripheral sympathetic nerve terminals as well as in tissues.
Entry Term	((2-Hexahydro-1(2H)-azocinyl)ethyl)guanidine
Entry Term	Guanethidine Monosulfate
Entry Term	Guanethidine Sulfate
Entry Term	Guanethidine Sulfate (1:2)
Entry Term	Guanethidine Sulfate (2:1)
Entry Term	Guanethidine Sulfate (2:1), 14C-Labeled
Entry Term	Ismelin
Entry Term	Isobarin
Entry Term	Octadine
Entry Term	Oktadin
Entry Term	Sulfate (1:1) of Guanethidine
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Adrenergic Agents
Pharm. Action	Antihypertensive Agents
Pharm. Action	Sympatholytics
CAS Type 1 Name	Guanidine, (2-(hexahydro-1(2H)-azocinyl)ethyl)-
Registry Number	55-65-2
Related Number	14920-15-1 (sulfate (1:2))
Related Number	60-02-6 (sulfate (2:1))
Related Number	645-43-2 (sulfate (1:1))
Related Number	87862-38-2 (sulfate (2:1), 14C-labeled)
Unique ID	D006145

MeSH Tree Structures

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MeSH Heading	Guanfacine
Tree Number	D02.078.370.465
Tree Number	D02.241.223.601.329
Scope Note	A centrally acting antihypertensive agent. The drug lowers both systolic and diastolic blood pressure by activating the central nervous system alpha-2 adrenoreceptors, which results in reduced sympathetic outflow leading to reduced vascular tone. Its adverse reactions include dry mouth, sedation, and constipation.
Entry Term	BS-100-141
Entry Term	Estulic
Entry Term	Guanfacine Hydrochloride
Entry Term	Guanfacine Monohydrochloride
Entry Term	Lon798
Entry Term	Tenex
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Adrenergic alpha-Agonists
Pharm. Action	Antihypertensive Agents
Pharm. Action	Sympatholytics
CAS Type 1 Name	Benzeneacetamide, N-(aminoiminomethyl)-2,6-dichloro-
Registry Number	29110-47-2
Related Number	29110-48-3 (mono-HCl)
Previous Indexing	Adrenergic alpha Agonists (1969-1990)
Previous Indexing	Antihypertensive Agents (1966-1990)
Previous Indexing	Guanidines (1966-1990)
Previous Indexing	Phenylacetates (1966-1990)
History Note	91
Unique ID	D016316

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MeSH Heading	Yohimbine
Tree Number	D03.132.973.641.893
Tree Number	D03.549.937.641.868
Scope Note	A plant alkaloid with alpha-2-adrenergic blocking activity. Yohimbine has been used as a mydriatic and in the treatment of impotence. It is also alleged to be an aphrodisiac.
Entry Term	Rauwolscine
Entry Term	Corynanthine
Entry Term	Corynanthine Tartrate
Entry Term	Yocon
Entry Term	Yohimex
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Adrenergic alpha-Antagonists
Pharm. Action	Mydriatics
CAS Type 1 Name	Yohimban-16-carboxylic acid, 17-hydroxy-, methyl ester, (16alpha,17alpha)-
Registry Number	146-48-5
Online Note	use YOHIMBINE /analogs & derivatives to search YOHIMBINE DERIVATIVES, CORYNANTHINE, & RAUWOLSCINE 1975-77; use YOHIMBANS 1969-74
History Note	YOHIMBINE DERIVATIVES was see under YOHIMBINE 1975-77, was see under YOHIMBANS 1969-74
Unique ID	D015016

MeSH Tree Structures

Heterocyclic Compounds [D03]
- Alkaloids [D03.132]
  - Yohimbans [D03.132.973]
    - Rauwolfia Alkaloids [D03.132.973.641]
      - Ajmaline [D03.132.973.641.119] +
      - Reserpine [D03.132.973.641.696]
      - ▶ Yohimbine [D03.132.973.641.893]

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MeSH Heading	Idazoxan
Tree Number	D03.383.231.388.425
Tree Number	D03.383.374.428
Scope Note	An alpha(2)-adrenoceptor antagonist. It has been used experimentally to test the binding activity of other chemicals.
Entry Term	RX-781094
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Adrenergic alpha-Antagonists
Registry Number	79944-58-4
Previous Indexing	Dioxanes (1985-1996)
Previous Indexing	Dioxins (1982-1984)
Previous Indexing	Imidazoles (1982-1996)
Online Note	use IDAZOXAN (NM) to search IDAZOXAN 1982-96
History Note	97; was IDAZOXAN (NM) 1982-96
Unique ID	D019329

MeSH Tree Structures

Heterocyclic Compounds [D03]
- Heterocyclic Compounds, 1-Ring [D03.383]
  - Dioxins [D03.383.231]
    - Dioxanes [D03.383.231.388]
      - ▶ Idazoxan [D03.383.231.388.425]